FOR OFFICIAL USE ONLY

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

25636

Examiner # (Mandatory): 76197 Requester's Full Name: Gail R. Gabel

Art Unit 1641 Location (Bldg/Room#): 7D16 Phone (circle) 305 306 308) 0807

Serial Number: 09/382,622 Results Format Preferred (circle): PAPER DISK E-MAIL

Title of Invention High Energy Phototerapeutic Agents

Inventors (please provide full names): H Craig Dees, Timothy Scott, John Smolik
Eric Wachter

Earliest Priority Date: 12198

Keywords (include any known synonyms registry numbers, explanation of initialisms):

Please search:

(1) halogenated xanthene
iodinated "
brominated "

(2) Rose Bengal
4,5,6,7-Tetrabromoerythrosin
* Claim 2 + Figure in last page *

(3) radiosensitizing agent
radiosensitizer
ionizing radiation
X ray
CAT scan
imaging contrast

Phloxine B
Erythrosin B
Eosin Y

(4) encapsulated delivery system (claim 11)

Search Topic:
Please write detailed statement of the search topic, and the concept of the invention. Describe as specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. You may include a copy of the abstract and the broadcast or most relevant claim(s).

(5) Target: tissue
cell membrane

RECEIVED
FEB 22 2
TECH CENTER 1600/2900

Point of Contact:
Mary Hale
Technical Info. Specialist
CM1 12D16 Tel: 308-4258

8.70

Abstract Attached

1413
(339-49
59
9

Thank You

STAFF USE ONLY

Searcher: Mary
Searcher Phone #:
Searcher Location:
Date Picked Up: 3.7
Date Completed: 3.9
Clerical Prep Time:
Online Time: 34
Databases:

Type of Search

_____ N.A. Sequence
_____ A.A. Sequence
_____ Structure (#)
✓ Bibliographic
_____ Litigation1
_____ Fulltext
_____ Procurement
_____ Other

Vendors (include cost where applicable)

STN
_____ Questel/Orbit
_____ Lexis/Nexis
_____ WWW/Internet
_____ In-house sequence systems (list)
_____ Dialog
_____ Dr. Link
_____ Westlaw
_____ Other

G. Gabel
382622

```
=> fil reg

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'REGISTRY' ENTERED AT 13:39:26 ON 09 MAR 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2000 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:    8 MAR 2000  HIGHEST RN 258533-18-5
DICTIONARY FILE UPDATES:   8 MAR 2000  HIGHEST RN 258533-18-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> e halogenated xanthane/cn 5

E1            1     HALOGENATED TYROSINE AMINOTRANSFERASE/CN
E2            1     HALOGENATED TYROSINE TRANSAMINASE/CN
E3            0 --> HALOGENATED XANTHANE/CN
E4            1     HALOGENE T 30/CN
E5            1     HALOHYDRIN DEHALOGENASE/CN

=> e rose bengal/cn 5

E1            1     ROSE B 1333/CN
E2            1     ROSE BD/CN
E3            1 --> ROSE BENGAL/CN
E4            1     ROSE BENGAL (131I) SODIUM/CN
E5            1     ROSE BENGAL 3-IODOPROPYL ESTER MONOSODIUM SALT/CN

=> s e3

L1            1 "ROSE BENGAL"/CN

=> fil medl,caplus,biosis,embase,wpids;s ((iodine or bromine or
halogenat?)(w)xanthene or l1 or (phloxine  or erythrosin)(w)b or eosin y or
rose bengal or tetrabromoerythrosin?) and (imag? contrast? or cat scan or
xray or x ray or imag?)

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         8.70       8.85

FILE 'MEDLINE' ENTERED AT 13:49:50 ON 09 MAR 2000

FILE 'CAPLUS' ENTERED AT 13:49:50 ON 09 MAR 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2000 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 13:49:50 ON 09 MAR 2000
COPYRIGHT (C) 2000 BIOSIS(R)
```

FILE 'EMBASE' ENTERED AT 13:49:50 ON 09 MAR 2000

FILE 'WPIDS' ENTERED AT 13:49:50 ON 09 MAR 2000

L2 381 FILE MEDLINE
L3 419 FILE CAPLUS
L4 71 FILE BIOSIS
L5 114 FILE EMBASE
L6 66 FILE WPIDS

TOTAL FOR ALL FILES
L7 1051 ((IODINE OR BROMINE OR HALOGENAT?)(W) XANTHENE OR L1 OR (PHLOXIN
E OR ERYTHROSIN)(W) B OR EOSIN Y OR ROSE BENGAL OR TETRABROMOERY
THROSIN?) AND (IMAG? CONTRAST? OR CAT SCAN OR XRAY OR X RAY OR IMAG?)

=> s l7 and (delivery vehicle or micelle or nanoparticle or liposome)

L8 0 FILE MEDLINE
L9 1 FILE CAPLUS
L10 0 FILE BIOSIS
L11 0 FILE EMBASE
L12 0 FILE WPIDS

TOTAL FOR ALL FILES
L13 1 L7 AND (DELIVERY VEHICLE OR MICELLE OR NANOPARTICLE OR LIPOSOME)

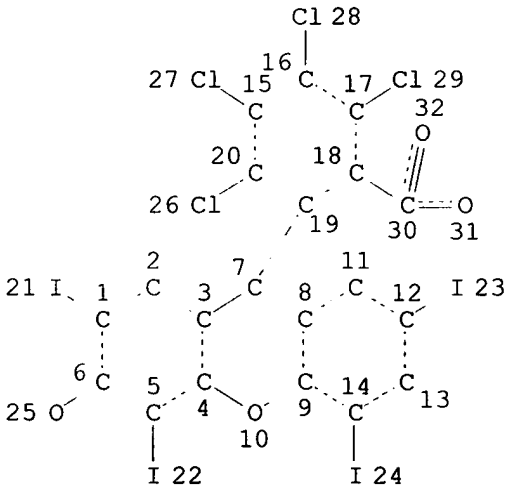
=> d cbib abs

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
1991:171315 Document No. 114:171315 Pharmaceutical compositions useful as drug **delivery vehicles** and/or as wound dressings.
Gibson, Mark; Taylor, Peter Mark; Payne, Nicholas Ian; Gould, Philip Leon (American Cyanamid Co., USA). Eur. Pat. Appl. EP 386960 A2 19900912, 27 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-302256 19900302. PRIORITY: JP 1989-50990 19890304; GB 1989-5138 19890307.
AB A pharmaceutical compn. comprises an aq. vehicle, a compd. having reversible thermosetting gel properties and a compd. having film-forming properties. Depending on the relative proportions of these components, the compn. can be adapted to function either as a vehicle for delivering pharmacol.- or diagnostically-active compds. to a human or animal patient and/or as a wound-dressing compn. The gel-former is polyoxyethylene-polyoxypropylene block copolymer or its derivs., and the film-former hydroxyethyl cellulose, hydroxypropyl Me cellulose or PVA. An ophthalmic compn. (pH 8.3; ethanolamine) comprised biphenylacetic acid ethanolamine salt 0.5, Pluronic F127 8.0, hydroxyethyl cellulose 8.0, sorbitol 2.5, benzalkonium chloride 0.01, borate buffer 2.0, and water to 100%.

=> s l7 and disease? tissue

L14 0 FILE MEDLINE

```
L15             0 FILE CAPLUS
L16             0 FILE BIOSIS
L17             0 FILE EMBASE
L18             0 FILE WPIDS

TOTAL FOR ALL FILES
L19             0 L7 AND DISEASE? TISSUE

=> fil reg

COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      58.83      67.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -0.56      -0.56

FILE 'REGISTRY' ENTERED AT 13:55:53 ON 09 MAR 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2000 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:    8 MAR 2000  HIGHEST RN 258533-18-5
DICTIONARY FILE UPDATES:   8 MAR 2000  HIGHEST RN 258533-18-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> d l22 que stat;d 1-5 ide cbib abs

L20             STR
```



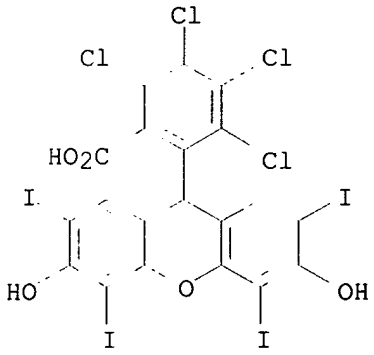

```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
```

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L22 5 SEA FILE=REGISTRY SSS FUL L20

100.0% PROCESSED 103 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

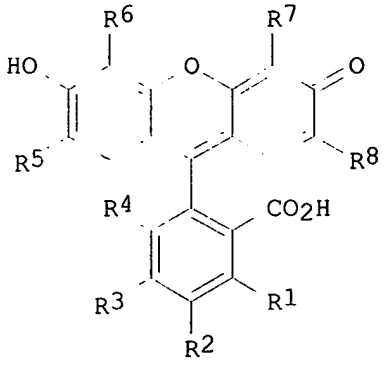
L22 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 202207-50-9 REGISTRY
CN Benzoic acid, 2,3,4,5-tetrachloro-6-(3,6-dihydroxy-2,4,5,7-tetraiodo-9H-xanthen-9-yl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H6 Cl4 I4 O5
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:136533 Xanthene dyes or derivatives as drugs for inducing ultrasonic action and apparatus wherein the drugs are used. Kawabata, Kenichi; Umemura, Shinichiro; Sasaki, Kazuaki; Sugita, Nami (Hitachi, Ltd., Japan; Kawabata, Kenichi; Umemura, Shinichiro; Sasaki, Kazuaki; Sugita, Nami). PCT Int. Appl. WO 9801131 A1 19980115, 62 pp. DESIGNATED STATES: W: CN, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1997-JP2285 19970702. PRIORITY: JP 1996-176207 19960705; JP 1997-31993 19970217.

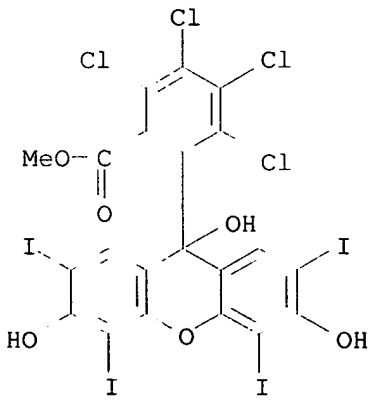
GI



I

AB Drugs contg. compds. of xanthene dyes or derivs. thereof (including dimers) having xanthene ring(s) and inducing an ultrasonic action of lowering the threshold of acoustic strength causing acoustic cavitation, (I) wherein any of R1 to R8 bonded to carbon atoms of the xanthene dye skeleton is a functional group capable of chem. binding to a halogeno, thiol or amino group (selected from among halogenated acetamide, maleimide, aziridine, isothiocyanate, succinimide and sulfonyl chloride). Because of being able to lower the threshold, these drugs make it possible to safely treat benign or malignant tumors or stones by the irradn. with ultrasonic waves of a low acoustic strength.

L22 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 134842-03-8 REGISTRY
CN Benzoic acid, 2,3,4,5-tetrachloro-6-(3,6,9-trihydroxy-2,4,5,7-tetraiodo-9H-xanthen-9-yl)-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H8 Cl4 I4 O6
SR CA
LC STN Files: CA, CAPLUS



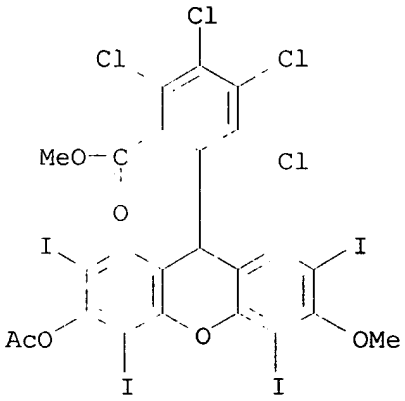
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:29976 Photochemical synthesis of nitroxyl free radicals in the presence of vinyl monomers. Van den Broeck, Hilde; Schmitz-Smets,

Maria; Smets, Georges (Lab. Macromol. Org. Chem., Kathol. Univ. Leuven, Louvain, B-3030, Belg.). J. Polym. Sci., Part A: Polym. Chem., 29(2), 201-8 (English) 1991. CODEN: JPACEC. ISSN: 0887-624X.

AB The photochem. formation of an inhibitor in the presence of monomers and a photoinitiator offered the possibility of producing pos. 2-step photoresists. As inhibitor precursors 2,2,6,6-tetramethylpiperidine and its 4-hydroxy deriv. were used in the presence of air oxygen and Rose Bengal as oxidn. photosensitizer. On irradn. with visible light (546 nm), stable nitroxyl radicals were formed, which acted as strong inhibitors of free radical polymn. Hexanediol diacrylate and diethylene glycol acrylate propionate were used as monomers. The photoinitiator required for the second step polymn. was benzoin iso-Pr ether, which photolyzed on irradn. at 340 nm. The quantum yield of nitroxyl radical formation was detd. in soln. and in polymeric films. Polymn. inhibition expts. were carried out with Me methacrylate in soln. and with neat monomers. Though the quantum yield was low, esp. in the last case, the expts. confirmed the possibilities of this 2-step procedure.

L22 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 115546-29-7 REGISTRY
CN Benzoic acid, 2-[3-(acetyloxy)-2,4,5,7-tetraiodo-6-methoxy-9H-xanthen-9-yl]-3,4,5,6-tetrachloro-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H12 Cl4 I4 O6
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



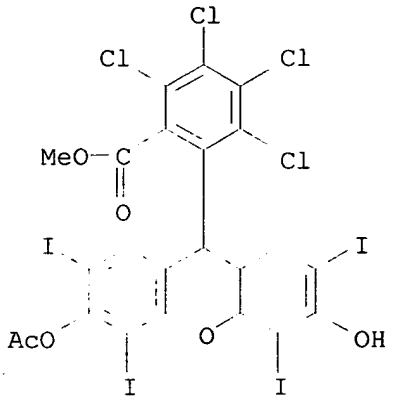
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:72793 Bleaching products of Rose Bengal under reducing conditions. Zakrzewski, Andrzej; Neckers, D. C. (Cent. Photochem. Sci., Bowling Green State Univ., Bowling Green, OH, 43403, USA). Tetrahedron, 43(20), 4507-12 (English) 1987. CODEN: TETRAB. ISSN: 0040-4020.

AB The bleaching behavior of Rose Bengal under reducing conditions was elucidated by detg. the products of chem. and photochem. redn. of Rose Bengal.

L22 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 115546-25-3 REGISTRY

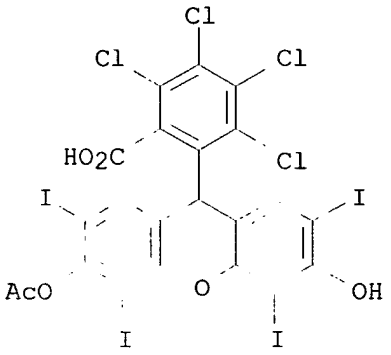
CN Benzoic acid, 2-[3-(acetyloxy)-6-hydroxy-2,4,5,7-tetraiodo-9H-xanthen-9-yl]-3,4,5,6-tetrachloro-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H10 Cl4 I4 O6
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:72793 Bleaching products of Rose Bengal under reducing conditions. Zakrzewski, Andrzej; Neckers, D. C. (Cent. Photochem. Sci., Bowling Green State Univ., Bowling Green, OH, 43403, USA). Tetrahedron, 43(20), 4507-12 (English) 1987. CODEN: TETRAB. ISSN: 0040-4020.
AB The bleaching behavior of Rose Bengal under reducing conditions was elucidated by detg. the products of chem. and photochem. redn. of Rose Bengal.

L22 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 115546-22-0 REGISTRY
CN Benzoic acid, 2-[3-(acetyloxy)-6-hydroxy-2,4,5,7-tetraiodo-9H-xanthen-9-yl]-3,4,5,6-tetrachloro-, disodium salt (9CI) (CA INDEX NAME)
MF C22 H8 Cl4 I4 O6 . 2 Na
SR CA
LC STN Files: CA, CAPLUS



● 2 Na

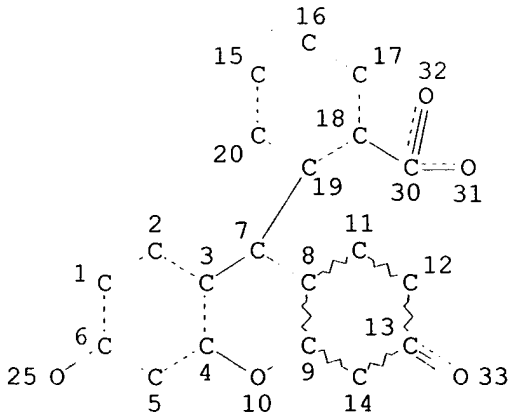
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:72793 Bleaching products of Rose Bengal under reducing conditions. Zakrzewski, Andrzej; Neckers, D. C. (Cent. Photochem. Sci., Bowling Green State Univ., Bowling Green, OH, 43403, USA). Tetrahedron, 43(20), 4507-12 (English) 1987. CODEN: TETRAB. ISSN: 0040-4020.

AB The bleaching behavior of Rose Bengal under reducing conditions was elucidated by detg. the products of chem. and photochem. redn. of Rose Bengal.

=> d l27 que stat;fil medl,caplus,biosis,embase;s l27 and (imag? or xray or x ray or cat scan or scan?)

L25 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
L27 613 SEA FILE=REGISTRY SSS FUL L25

100.0% PROCESSED 2661 ITERATIONS 613 ANSWERS
SEARCH TIME: 00.00.01

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	271.05	338.73

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.65	-3.21

FILE 'MEDLINE' ENTERED AT 14:00:12 ON 09 MAR 2000

FILE 'CAPLUS' ENTERED AT 14:00:12 ON 09 MAR 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 14:00:12 ON 09 MAR 2000

FILE 'EMBASE' ENTERED AT 14:00:12 ON 09 MAR 2000

L28 548 FILE MEDLINE
L29 694 FILE CAPLUS
L30 651 FILE BIOSIS
L31 589 FILE EMBASE

TOTAL FOR ALL FILES
L32 2482 L27 AND (IMAG? OR XRAY OR X RAY OR CAT SCAN OR SCAN?)

=> s l32 and (delivery vehicle or micelle or nanoparticle or liposome or inject? or flood? or spray?)

L33 79 FILE MEDLINE
L34 50 FILE CAPLUS
L35 56 FILE BIOSIS
L36 87 FILE EMBASE

TOTAL FOR ALL FILES
L37 272 L32 AND (DELIVERY VEHICLE OR MICELLE OR NANOPARTICLE OR LIPOSOME
OR INJECT? OR FLOOD? OR SPRAY?)

=> s l37 and (treat? or therap?) and (cell membrane or tissue)

L38 6 FILE MEDLINE
L39 3 FILE CAPLUS
L40 1 FILE BIOSIS
L41 9 FILE EMBASE

TOTAL FOR ALL FILES
L42 19 L37 AND (TREAT? OR THERAP?) AND (CELL MEMBRANE OR TISSUE)

=> dup rem l42

PROCESSING COMPLETED FOR L42
L43 18 DUP REM L42 (1 DUPLICATE REMOVED)

=> d 1-18 cbib abs;s dees h?/au;s scott t?/au;s smolik j?/au;s wachter e?/au

L43 ANSWER 1 OF 18 MEDLINE
2000100374 Document Number: 20100374. Angiography of fluorestricted anti-vascular endothelial growth factor antibody and dextrans in experimental choroidal neovascularization. Tolentino M J; Husain D; Theodosiadis P; Gragoudas E S; Connolly E; Kahn J; Cleland J; Adamis A P; Cuthbertson A; Miller J W. (Retina Service, Massachusetts Eye and Ear Infirmary, Boston 02114, USA.) ARCHIVES OF OPHTHALMOLOGY, (2000 Jan) 118 (1) 78-84. Journal code: 830. ISSN: 0003-9950. Pub. country: United States. Language: English.

AB OBJECTIVE: To determine if anti-vascular endothelial growth factor antibody and a range of dextrans with varying diffusion radii and molecular weights are permeable through experimental choroidal neovascularization (CNV). METHODS: Choroidal neovascularization was induced in 10 cynomolgus monkey retinas by means of argon laser injury. Digital fundus fluorescein angiograms were performed with fluorescein sodium, fluoresceinated IgG antibodies (anti-vascular endothelial growth factor and a control antibody), and fluoresceinated dextrans with molecular weights of 4, 20, 40, 70 and 150 kd. The 40- and 70-kd dextrans straddle the effective diffusion radius of IgG. For each reagent, early and late angiograms were performed in a standardized fashion, with follow-up **images** obtained to monitor residual fluorescence. RESULTS: Perfusion of retinal vessels and choroidal vasculature was seen with all reagents. Fluorescein and 4- and 20-kd dextran leaked rapidly from the CNV within the first minute. Angiography with the use of 40-kd dextran and fluoresceinated antibody, either anti-vascular endothelial growth factor or control IgG, showed fluorescence within the CNV that increased during the first 1 to 5 hours, with mild leakage from the CNV. By 24 hours, fluorescence in the CNV was minimal, although in some cases persistent fluorescence in the surrounding **tissue** was evident up to 2 weeks. The 70-kd dextran showed fluorescence within the CNV and leakage in 1 of 3 eyes. The 150-kd dextran showed fluorescence within the CNV but did not demonstrate leakage. CONCLUSIONS: Fluoresceinated antibodies and dextran with smaller effective diffusion radii showed CNV perfusion and leakage. Dextrans with larger effective diffusion radii (70 kd and 150 kd) perfused into CNV but did not show leakage consistently. CLINICAL RELEVANCE: Determining the permeablity of antibodies and molecules of similar size through CNV can help ascertain the feasibility of using intravenously administered antibodies against angiogenic growth factors as a future **treatment** for choroidal neovascularization.

L43 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2000 ACS
1999:404815 Document No. 131:56154 Optoacoustic contrast agents and methods for their use in ultrasound and optical **imaging**. Unger, Evan C.; Wu, Yunqiu (Imarx Pharmaceutical Corp., USA). PCT Int. Appl. WO 9930620 A1 19990624, 166 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US27060 19981217. PRIORITY: US 1997-993165 19971218.

AB The present invention generally relates to optoacoustic contrast agents and methods of diagnostic and **therapeutic imaging** using optoacoustic contrast agents. A compn. comprising a stabilizing material and a photoactive agent is administered and the patient is

scanned using ultrasound **imaging** and optical **imaging** to obtain visible **images** of a region of the patient. The compns. may comprise a wide variety of addnl. components, including, for example, one or more of gases, gaseous precursors, liqs. oils, stabilizing materials, diagnostic agents, photoactive agents, bioactive agents, and/or targeting ligands. Perfluoropropane encapsulated optoacoustic **liposomes** were formed from dipalmitoylphosphatidylcholine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylethanolamine-PEG 5,000, and dipalmitoylphosphatidylethanolamine derivatized with lissamine rhodamine B. The sized photoactive lipid was optimally excited with 550 nm light and the fluorescence emission peak was 590 nm.

L43 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2000 BIOSIS
1999:338348 Document No.: PREV199900338348. Angiographic and histologic effects of fundus photodynamic **therapy** with a hydrophilic sensitizer (mono-L-aspartyl chlorin e6. Mori, Keisuke; Yoneya, Shin; Ohta, Masataka; Sano, Akemi; Anzai, Kaname; Peyman, Gholam A. (1); Moshfeghi, Darius M.. (1) LSU Eye Center, 2020 Gravier St., Suite B, New Orleans, LA, 70112-2234 USA. Ophthalmology, (July, 1999) Vol. 106, No. 7, pp. 1384-1391. ISSN: 0161-6420. Language: English. Summary Language: English.
AB Purpose: To demonstrate the efficacy of the photosensitizer mono-L-aspartyl chlorin e6 (NPe6) in closing choroidal vessels at low energy levels, that **tissue** uptake and clearance are rapid, and that low concentrations of drug are needed to achieve clinical effects. Design: Experimental animal study. Animals: Pigmented rabbits and Japanese monkeys were used in this study. Methods: Using a modified 664-nm diode laser, the fundi of pigmented rabbits and Japanese monkeys were irradiated after intravenous administration of NPe6 (2-100 mg/kg). Time from **injection** to irradiation varied from 5 to 15 minutes, and duration of exposure varied from 1 to 10 seconds. Power output at the corneal surface was either 3.6 or 5.9 mW. Animals were examined by indirect ophthalmoscopy and fluorescent angiography at 2 hours and 7 days after **treatment**. After enucleation 7 days after **treatment**, specimens were prepared for light and electron microscopy. Main Outcome Measures: Angiographic evidence of occlusion and histopathologic evidence of retinal damage. Results: Both clinical and histopathologic examination demonstrated effects on the choroidal vasculature and the retinal pigment epithelium, including necrosis of endothelial cells and occlusion in choroidal vessels, particularly within the choriocapillaris, at low energy levels. Overlying neurosensory retina was minimally affected. Fluorescein angiography of lesions **treated** with 2 mg/kg and laser fluence of 2.3 to 7.5 J/cm2 showed a normal appearance 2 hours after **treatment**, which changed to early hypofluorescent and later hyperfluorescent lesions 7 days after **treatment**. In contrast, those animals receiving the 10-mg/kg dose and laser fluence of 0.46 to 0.75 J/cm2 showed marked hypofluorescence of choroidal lesions and occlusion of retinal vessels 7 days after **treatment**. Conclusions: Effective occlusion of normal choroidal vessels was achieved at 2 mg/kg using 2.3 to 7.5 J/cm2 or at 10 mg/kg using 0.46 to 0.75 J/cm2 with minimal injury to overlying neurosensory retina.

L43 ANSWER 4 OF 18 MEDLINE
1999432367 Document Number: 99432367. Cellular penetration of fluorescently

labeled superoxide dismutases of various origins. Filipe P; Emerit I; Vassy J; Levy A; Huang V; Freitas J. (Institut Sante et Developpement, Universite Pierre et Marie Curie, Paris, France.) MOLECULAR MEDICINE, (1999 Aug) 5 (8) 517-25. Journal code: CG3. ISSN: 1076-1551. Pub. country: United States. Language: English.

AB BACKGROUND: Using fluorescently labeled superoxide dismutase (SOD) and flow cytometry, we have shown previously that the enzyme CuZn SOD (EC 1.15.1.1) from bovine erythrocytes binds rapidly to the cell surface with slow uptake into the cell during the following hours. The degree of labeling was most important for monocytes in comparison to other blood cells (erythrocytes, lymphocytes, and neutrophils) and fibroblasts. In agreement with the flow-cytometric findings, the inhibition of superoxide production was more important for SOD-pretreated monocytes than for neutrophils, as demonstrated with the cytochrome c reduction assay. It was thus of interest to confirm the observed differences between monocytes and neutrophils with confocal laser microscopy, study in greater detail the kinetics of binding, penetration, and intracellular localization of the enzyme, and compare the results obtained with bovine CuZn SOD with those from SODs of other origins and carrying different active sites. MATERIALS AND METHODS: Recombinant human (rh), bovine, and equine CuZn SODs, as well as rh and E. coli Mn SODs, were studied before use with respect to specific activity and purity (HPLC, SDS-PAGE electrophoresis). Fluorescein isothiocyanate was covalently conjugated to the various SODs for study with high-resolution confocal **scanning** laser microscopy. Superoxide production by monocytes and neutrophils was measured with the cytochrome c assay. RESULTS: As expected from our experiments with flow cytometry, only rare neutrophils were labeled with FITC-SOD, even with the longest incubation time of 3 hr and the highest dose of 1500 units/ml. In addition, they showed a localized fluorescence pattern that was quite different from the diffuse punctate fluorescence pattern of monocytes. Lymphocytes were not labeled at all. The rapid binding to the cellular surface of monocytes was confirmed, and even after 5 min of preincubation, FITC-SOD was found on a small percentage of monocytes. This was correlated with a reduction in superoxide release after phorbolmyristate acetate (PMA) stimulation by 40%. An interesting finding was the perinuclear accumulation of the penetrated SOD after the longest pretreatment of 3 hr, suggesting a barrier against further progression. Indeed, through confocal microscopy we were able to exclude any fluorescence at the nuclear level. While the fluorescence labeling patterns and the kinetics of penetration were quite similar for bovine, equine, and rh CuZn SOD, the Mn SODs showed poor labeling, correlated with a weak inhibitory effect on cytochrome c reduction, which was not statistically significant. CONCLUSIONS: The rapid binding of native CuZn SODs on the surface of monocytes, leading to reduced superoxide release by these cells, explains the observation that beneficial effects of **injected** SOD lasted for months despite rapid clearance of the enzyme from the bloodstream, according to pharmacodynamic studies. The preferential binding to monocytes, in contrast to neutrophils, may play a role in chronic inflammatory diseases in which the monocytes are in an activated state. The differences in binding capacity between CuZn SODs and Mn SODs, correlated with different

inhibitory effects of superoxide production by monocytes, may also have **therapeutic** significance.

L43 ANSWER 5 OF 18 MEDLINE DUPLICATE 1
1999131774 Document Number: 99131774. **Imaging** of apoptosis (programmed cell death) with 99mTc annexin V. Blankenberg F G; Katsikis P D; Tait J F; Davis R E; Naumovski L; Ohtsuki K; Kopiwoda S; Abrams M J; Strauss H W. (Department of Radiology, Stanford University School of Medicine, California 94305, USA.) JOURNAL OF NUCLEAR MEDICINE, (1999 Jan)
40 (1) 184-91. Journal code: JEC. ISSN: 0161-5505. Pub. country: United States. Language: English.
AB Apoptosis (programmed cell death) is a critical element in normal physiology and in many disease processes. Phosphatidylserine (PS), one component of **cell membrane** phospholipids, is normally confined to the inner leaflet of the plasma membrane. Early in the course of apoptosis, this phospholipid is rapidly exposed on the cell's outer surface. Annexin V, an endogenous human protein, has a high affinity for membrane-bound PS. This protein has been labeled with fluorescein and has been used to detect apoptosis in vitro. We describe the use of radiolabeled annexin V to detect apoptosis in vivo. The results are compared to histologic and flow cytometric methods to identify cells and **tissues** undergoing apoptosis. METHODS: Annexin V was coupled to hydrazinonicotinamide (HYNIC) and radiolabeled with 99mTc. Bioreactivity of 99mTc-HYNIC annexin V was compared with fluorescein isothiocyanate (FITC)-labeled annexin V in cultures of Jurkat T-cell lymphoblasts and in ex vivo thymic cell suspensions undergoing apoptosis in response to different stimuli. In addition, the uptake of FITC annexin V and 99mTc-HYNIC annexin V was studied in heat-**treated** necrotic Jurkat T-cell cultures. In vivo localization of annexin V was studied in Balb/c mice **injected** with 99mTc-HYNIC annexin V before and after induction of Fas-mediated hepatocyte apoptosis with intravenously administered antiFas antibody. RESULTS: Membrane-bound radiolabeled annexin V activity linearly correlated to total fluorescence as observed by FITC annexin V flow cytometry in Jurkat T-cell cultures induced to undergo apoptosis in response to growth factor deprivation (N = 10, r2 = 0.987), antiFas antibody (N = 8, r2 = 0.836) and doxorubicin (N = 10, r2 = 0.804); and in ex vivo experiments on thymic cell suspensions with dexamethasone-induced apoptosis from Balb/c mice (N = 6, r2 = 0.989). Necrotic Jurkat T-cell cultures also demonstrated marked increases in radiopharmaceutical (4000-5000-fold) above control values. AntiFas antibody-**treated** Balb/c mice (N = 6) demonstrated a three-fold rise in hepatic uptake of annexin V (P < 0.0005) above control (N = 10), identified both by **imaging** and scintillation well counting. The increase in hepatic uptake in antiFas antibody-**treated** mice correlated to histologic evidence of fulminant hepatic apoptosis. CONCLUSION: These data suggest that 99mTc-HYNIC annexin V can be used to **image** apoptotic and necrotic cell death in vivo.

L43 ANSWER 6 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
1999170458 EMBASE Calpain inhibitor entrapped in **liposome** rescues ischemic neuronal damage. Yokota M.; Tani E.; Tsubuki S.; Yamaura I.; Nakagaki I.; Hori S.; Saido T.C.. M. Yokota, Department of Neurosurgery, Hyogo College of Medicine, Mukogawacho 1-1, Nishinomiya, Hyogo 663, Japan.
yoko-ns@hyo-med.ac.jp. Brain Research 819/1-2 (8-14) 20 Feb 1999.
Refs: 31.
ISSN: 0006-8993. CODEN: BRREAP.
Publisher Ident.: S 0006-8993(98)01334-1. Pub. Country: Netherlands.
Language: English. Summary Language: English.

AB Transient forebrain ischemia induces activation of calpain and proteolysis of a neuronal cytoskeleton, fodrin, in gerbil hippocampus. This phenomenon precedes delayed neuronal death in hippocampal CA1 neurons. We examined effects of a calpain inhibitor on delayed neuronal death after transient forebrain ischemia. In gerbils, a selective calpain inhibitor entrapped in **liposome** was given transvenously and 30 min later, 5-min forebrain ischemia was produced by occlusion of both common carotid arteries. On day 7, CA1 neuronal damage was examined in the hippocampal slices stained with cresyl violet. Calpain-induced proteolysis of fodrin was also examined by immunohistochemistry and immunoblot. Additionally, to assure entrapment of the inhibitor by CA1 neurons, the inhihitor-**liposome** complex was labeled with FITC and given to gerbils. Fluorescence in the hippocampal slices was examined by confocal laser **scanning** microscope. Selective CA1 neuronal damage induced by forebrain ischemia was prevented by administration of the inhibitor in a dose-dependent manner. Calpain-induced proteolysis of fodrin was also extinguished by the calpain inhibitor in a dose-dependent manner. Bright fluorescence of the FITC-labeled inhibitor was observed in the CA1 neurons. The data show an important role of calpain in the development of the ischemic delayed neuronal death. Calpain seems to produce neuronal damage by degrading neuronal cytoskeleton. Our data also show a palliative effect of the calpain inhibitor on the neurotoxic damage, which offers a new and potent **treatment** of transient forebrain cerebral ischemia.

L43 ANSWER 7 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

1998409363 EMBASE Vascular permeability in experimental diabetes is associated with reduced endothelial occludin content. Vascular endothelial growth factor decreases occludin in retinal endothelial cells. Antonetti D.A.; Barber A.J.; Khin S.; Lieth E.; Tarbell J.M.; Gardner T.W.. Dr. T.W. Gardner, Penn State Geisinger Health System, Penn State University Coll. of Med., Ulerich Ophthalmology Research Ctr., 500 University Dr., Hershey, PA 17033, United States. tgardner@psghs.edu. Diabetes 47/12 (1953-1959) 1998.

Refs: 44.

ISSN: 0012-1797. CODEN: DIAEAZ. Pub. Country: United States. Language: English. Summary Language: English.

AB Blood-retinal barrier (BRB) breakdown is a hallmark of diabetic retinopathy, but the molecular changes that cause this pathology are unclear. Occludin is a transmembrane component of interendothelial tight junctions that may regulate permeability at the BRB. In this study, we examined the effects of vascular endothelial growth factor (VEGF) and diabetes on vascular occludin content and barrier function. Sprague-Dawley rats were made diabetic by intravenous streptozotocin **injection**, and age-matched animals served as controls. After 3 months, BRB permeability was quantified by intravenous **injection** of fluorescein isothiocyanate-bovine serum albumin (FITC-BSA), M(r) 66 kDa, and 10-kDa rhodamine-dextran (R-D), followed by digital **image** analysis of retinal sections. Retinal fluorescence intensity for FITC-BSA increased 62% (P .ltoreq. 0.05), but R-D fluorescence did not change significantly. Occludin localization at interendothelial junctions was

confirmed by immunofluorescence, and relative protein content was determined by immunoblotting of retinal homogenates. Retinal occludin content decreased .apprx.35% ($P < 0.03$) in the diabetic versus the control animals, whereas the glucose transporter GLUT1 content was unchanged in rat retinas. Additionally, **treatment** of bovine retinal endothelial cells in culture with 0.12 nmol/l or 12 nmol/l VEGF for 6 h reduced occludin content 46 and 54%, respectively. These data show that diabetes selectively reduces retinal occludin protein expression and increases BRB permeability. Our findings suggest that the elevated VEGF in the vitreous of patients with diabetic retinopathy increases vascular permeability by downregulating occludin content. Decreased tight junction protein expression may be an important means by which diabetes causes increased vascular permeability and contributes to macular edema.

L43 ANSWER 8 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

1998123795 EMBASE Simultaneous indocyanine green and fluorescein angiography using a confocal **scanning** laser ophthalmoscope. Freeman W.R.; Bartsch D.-U.; Mueller A.J.; Banker A.S.; Weinreb R.N.. Dr. W.R. Freeman, UCSD Shiley Eye Center, 9415 Campus Point Dr, San Diego, CA 92093-0946, United States. Archives of Ophthalmology 116/4 (455-463) 1998.
Refs: 25.
ISSN: 0003-9950. CODEN: AROPAW. Pub. Country: United States. Language: English. Summary Language: English.

AB Background: Fluorescein and indocyanine green (ICG) angiography are both useful in the diagnosis and **treatment** of many retinal diseases. In some cases, both tests must be performed for diagnosis and **treatment**; however, performing both is time-consuming and may require multiple **injections**. Methods: We designed a compact digital confocal **scanning** laser ophthalmoscope to perform true simultaneous fluorescein and ICG angiography. We report our experience using the instrument to perform 169 angiograms in 117 patients. Results: There were no unexpected adverse effects from mixing the dyes and administering them in 1 **injection**. An entire examination, including fundus photography, fluorescein angiography, and ICG angiography, could be performed in 45 minutes. It was possible to study differences in fluorescein patterns by comparing identically timed frames and to find cases in which ICG or fluorescein was optimal in visualizing retinal and subretinal structures. Confocal optical sections in the depth (z) dimension allowed viewing in different planes. It was possible to overlay ICG and fluorescein **images** or compare them side-by-side using a linked cursor. Digital transmission of the **images** was also performed. Conclusions: Simultaneous ICG and fluorescein angiography can be performed rapidly, safely, and conveniently. The availability of simultaneous angiography will allow critical determination of the relative advantages and disadvantages of both types of angiography.

L43 ANSWER 9 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

97262315 EMBASE Document No.: 1997262315. Photochemically-induced vascular damage in brain cortex. Transmission and **scanning** electron microscopy study. Gajkowska B.; Frontczak-Baniewicz M.; Gadamski R.; Barskov I.. B. Gajkowska, LUCNS, Medical Research Centre, Polish Academy of Sciences, 5 Pawinski St, 02-106 Warsaw, Poland. Acta Neurobiologiae Experimentalis 57/3 (203-208) 1997.
Refs: 20.
ISSN: 0065-1400. CODEN: ANEXAC. Pub. Country: Poland. Language: English. Summary Language: English.

AB Morphological changes of microvessels of cerebral cortex were evaluated in

a model of cerebral infarction initiated by a photochemical reaction. Rats were **treated** with intravenous **injection** of rose Bengal and irradiated from a halogen lamp source through an intact cranium to precipitate microvascular damage. Investigations in transmission and **scanning** electron microscopy revealed platelet aggregation on endothelial cells preceded by its early ultrastructural damage. Other typical microscopic features of brain ischaemic injury were present suggesting that the present method may be used as a model for investigating ischaemic brain damage. Since the photochemical activation of the rose Bengal dye results in formation of reactive oxygen species this model may be particularly useful to elucidate the role of free radical- mediated endothelial damage in the formation of microthrombi and blood- brain-barrier integrity.

L43 ANSWER 10 OF 18 MEDLINE
97013060 Document Number: 97013060. Intracarotid tumor necrosis factor-alpha administration increases the blood-brain barrier permeability in cerebral cortex of the newborn pig: quantitative aspects of double-labelling studies and confocal laser **scanning** analysis. Abraham C S; Deli M A; Joo F; Megyeri P; Torpier G. (Department of Pediatrics, Albert Szent-Gyorgyi Medical University, Szeged, Hungary.. abraham@pedia.szote.u-szeged.hu) . NEUROSCIENCE LETTERS, (1996 Apr 19) 208 (2) 85-8. Journal code: N7N. ISSN: 0304-3940. Pub. country: Ireland. Language: English.
AB Tumor necrosis factor-alpha (TNF-alpha) plays a crucial role in the pathogenesis of the central nervous system infections. The aim of the present study was to analyze quantitatively the changes in the blood-brain barrier (BBB) permeability after the intracarotid **injection** of TNF-alpha. Recombinant human TNF-alpha was **injected** into the left internal carotid artery of anesthetized newborn pigs (n = 48) in the doses of 0, 1000, 10 000 and 100 000 IU, respectively. Before, as well as 1, 2, 4, 8, and 16 h after the challenge, the extravasation of a small (sodium fluorescein (SF), mw 376), and a large (Evan's blue-albumin (EBA), mw 67 000) tracer was determined concomitantly by spectrophotometry in the cerebral cortex of the animals. There was a time- and dose-dependent increase in BBB permeability both for SF and EBA; however, significant ($P < 0.05$) BBB opening for albumin only developed 2 h after the challenge. In the morphological study the same excitable tracers, identical experimental protocol and groups were used. Cryostat sections of brain **tissue** were viewed for optical sectioning with a confocal laser **scanning** microscope equipped with an argon/krypton ion laser. A diffuse BBB opening for SF and a moderate perivascular extravasation for EBA were found in the cortices of TNF-alpha-**treated** animals. We conclude that significant increases in intravascular TNF-alpha-concentration during neonatal infections may result in vasogenic brain edema formation.

L43 ANSWER 11 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
96263938 EMBASE Document No.: 1996263938. Nerve growth factor delays retinal degeneration in C3H mice. Lambiase A.; Aloe L.. Institute of Neurobiology, CNR, Viale Marx 15,I-00137 Rome, Italy. Graefe's Archive for Clinical and Experimental Ophthalmology 234/SUPPL. 1 (S96-S100) 1996.

ISSN: 0721-832X. CODEN: GACODL. Pub. Country: Germany. Language: English. Summary Language: English.

AB Background: The aim of the present study was to investigate the biological role of nerve growth factor (NGF) on retinal degeneration in the C3H mouse strain. This strain is characterized by a single gene mutation (rd) which leads to photoreceptor degeneration resembling human retinitis pigmentosa.

Methods: Neural retinas from 1- to 25 day-old C3H mice were dissected from outer ocular **tissues**, dissociated in cell suspension, stained with a vital dye and counted in a hemocytometer. For in vivo study, NGF was **injected** into the intraocular or retro-ocular area, and at the end of the **treatment** the mice were killed. The eyes were enucleated, fixed and cut by cryostat into 14-.mu.m serial sections. The serial sections were stained with hematoxylin-eosin and the outer nuclear layer (ONL) was measured using a computerized **image** analysis system. Results: An intraocular **injection** of NGF, or repeated retro-ocular **injections**, induced a significant increase in ONL thickness compared to controls. Conclusion: Our data show that NGF inhibits retinal degeneration in C3H mice. The mechanism(s) underlying the protective action of NGF against retinal cell death remains to be established.

L43 ANSWER 12 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

96365465 EMBASE Document No.: 1996365465. Noninvasive monitoring of intraocular pharmacokinetics of daunorubicin using fluorophotometry. Kizhakkethara I.; Li X.; El-Sayed S.; Khoobehi B.; Moshfeghi D.M.; Rahimy M.; Peyman G.A.. LSU Eye Centre, State University Medical Center, School of Medicine,New Orleans, LA 70112-2234, United States. International Ophthalmology 19/6 (363-367) 1995.

ISSN: 0165-5701. CODEN: INOPDR. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB Purpose. Daunorubicin is a cytotoxic drug, which, in nontoxic doses, is effective in preventing cellular proliferation in experimental vitreoretinopathy. We studied dose and clearance of daunorubicin in various ocular **tissues** using fluorophotometry techniques.

Methods. In vitro tests: The emission of fluorescence from the daunorubicin solution having a concentration range of 0.1 to 10 .mu.g/mL in phosphate buffer was measured using an excitation wavelength range of 489 .+-. 10 nm. The emission of fluorescence was measured at 514 nm; the linearity of the response was determined using linear regression analysis.

There is a fluorescence peak of daunorubicin at 485 nm. The validity and reproducibility of the method were examined. In vivo tests: The rabbits were randomized into three groups and daunorubicin concentrations of 4, 6, or 8 .mu.g/mL were **injected** into the vitreous. Fluorophotometry **scanning** from the retina to the anterior chamber was performed with a commercially available fluorophotometer at various times up to 48 hours after **injection** to quantify fluorescence emission of daunorubicin. Results. The standard curve of fluorescence versus concentration of daunorubicin was linear in the range of 0.1 to 8 .mu.g/mL. It was sensitive up to 0.1 .mu.g. The daunorubicin time concentration profile showed a dose response relationship over the 48-hour period studied. The half-life of daunorubicin in the vitreous was about 5 hours. Conclusion. We Performed fluorophotometry using a fluorophotometer whose exciter emits light at 489 nm, which is very close to an absorption

peak of daunorubicin. These two values are close enough to obviate the need for modifying the commercial fluorophotometer. Therefore the concentration of daunorubicin in the vitreous cavity can be measured noninvasively.

L43 ANSWER 13 OF 18 MEDLINE
96124257 Document Number: 96124257. Increased capillary endothelial leakage in portal hypertensive gastric mucosa: fluorescence microscopy in CCl4-induced cirrhotic rats. Kotzampassi K; Karkavelas G; Eleftheriadis E;
Papadimitriou C; Aletras H. (Department of Surgery, University of Thessaloniki, Greece.) RESEARCH IN EXPERIMENTAL MEDICINE, (1995) 195 (3) 145-52. Journal code: R67. ISSN: 0300-9130. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.
AB Since portal hypertension affects the gastric mucosa, leading to congestive gastropathy and thus to increased incidence of bleeding, it is one of the possible causes of increased permeability of gastric mucosal capillaries. The aim of this study was the quantitative assessment of the permeability of the gastric mucosal endothelial cells. Eight CCl4-induced cirrhotic rats and eight matched controls were subjected to i.v. **injection** of FITC-albumin, and a morphometric evaluation of fluorescence in serial histological sections of the gastric mucosa was performed by a video **image** analysis system. Fluorescence was found to be 0.351 +/- 0.01% of the area **scanned** in experimental animals versus 0.073 +/- 0.005% in controls, i.e. it was significantly increased by the **treatment**, which implies a significant endothelial leakage into the extravascular space.

L43 ANSWER 14 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
95254286 EMBASE Document No.: 1995254286. Topographical evaluation of skin perfusion patterns in peripheral arterial occlusive disease by means of computer-assisted fluorescein perfusography. Scheffler A.; Rieger H.. Aggertallklinik,W-51766 Engelskirchen, Germany. European Journal of Vascular and Endovascular Surgery 10/1 (60-68) 1995.
ISSN: 1078-5884. CODEN: EJVSFZ. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB Objective: To evaluate the clinical impact of computer-assisted fluorescein perfusography in peripheral arterial occlusive disease (PAOD).
Design: Foot and calf skin perfusion was visualised by intravenous fluorescsin **injection**. Fluorescein influx was recorded photographically and converted into functional **images** of fluorescein appearance times (AT) by means of digital film processing. Setting: Vascular Laboratory of Clinic for Vascular Disease. Materials: 249 patients with PAOD. Among 481 limbs studied, 83 legs presented with patent arteries, 70 with asymptomatic obstructions (Stage I), 170 with claudication (Stage II) and 158 with rest pain and skin lesions (Stage III/IV). Chief outcome measures: Forefoot and calf mean ATs and standard deviations (SD) served as arbitrary measures of regional skin perfusion rates and their homogeneity, respectively. Main results: In the control legs, a homogeneous and fast fluorescence appearance was observed (medians
at the foot: AT 33.4 s, SD 3.6). In stage II disease, AT (39.9 s, SD 5.6) were slightly impaired as compared to limbs with patent arteries or stage I disease ($p<0.01$). Ninety-seven out of the 158 legs in stage III/IV could
be managed by conservative **therapy**. According to fluoressein-perfusography, they did not differ from stage II disease (AT 38.8 s, SD 6.1). Sixty-one limbs were clinically affected by critical ischaemia. They exhibited a markedly delayed and heterogeneous fluorescein

influx at the foot (AT 77.3 s, SD 26.5, p<0.01 vs all other groups). Non-fluorescent areas occured in 53% compared to only 1% of limbs with and without critical ischaemia, respectively. Retrospectively, predictive values of fluorescein perfusography in identifying a critical limb ischaemia (accuracy 93%) were superior to the ankle systolic arterial pressure determination (accuracy 80%). Conclusions: Fluorescein perfusography seems to be of diagnostic and prognostic use in PAOD in stage III/IV where inflammatory and ischaemic patterns of dye appearance can be distinguished.

L43 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2000 ACS
1994:211644 Document No. 120:211644 System for delivery of diagnostic or **therapeutic** agents to the lymphatic **tissues**. Papisov, Mikhail I.; Brady, Thomas J. (General Hospital Corp., USA). PCT Int. Appl. WO 9402068 A1 19940203, 80 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US6848 19930721. PRIORITY: US 1992-917707 19920721.
AB A substance for diagnosis or **therapy** of an animal includes an agent which is detectable or **therapeutically** active, the agent being linked to a carrier which is linked to a targeting site, whereby the agent accumulates in the lymphatic system of the animal to a greater degree than if the targeting site were absent. The carrier is e.g. a polypeptide or polysaccharide or other polymer; the targeting site is e.g. a carbohydrate (dextran, starch, etc.). Dextran-grafted poly-L-lysine[111In-DTPA] (synthesis protocol described) was **injected** into rats and rabbits and .gamma.-scintigraphic **images** were obtained. Prepn. and testing of other dextran-grafted polylysine derivs. are also described.

L43 ANSWER 16 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
94028354 EMBASE Document No.: 1994028354. Effect of 21-aminosteroid lipid peroxidation inhibitor, U74006F, in the rat middle cerebral artery occlusion model. Umemura K.; Wada K.; Uematsu T.; Mizuno A.; Nakashima M..
Department of Pharmacology, Hamamatsu University School Medicine, 3600 Handa-cho,Hamamatsu 431-31, Japan. European Journal of Pharmacology 251/1 (69-74) 1994.
ISSN: 0014-2999. CODEN: EJPHAZ. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB The aim of this study was to evaluate the effect of 21 -aminosteroid lipid peroxidation inhibitor, U74006F, on ischaemic brain **tissue** damage using the rat middle cerebral artery occlusion model. Under anaesthesia, the left middle cerebral artery was exposed without cutting the dura mater via a subtemporal craniotomy, under an operating microscope. Photo-illumination (wave length; 540 nm) was applied to the middle cerebral artery and then rose bengal (20 mg/kg) was administered intravenously. The middle cerebral artery was completely occluded by thrombus about 6 min after the administration of rose bengal. U74006F (1.0 mg/kg) was then **injected** intravenously just after the cessation of illumination. Twenty four hours after the operation, the extent of ischaemic damage was measured by magnetic resonance **imaging** technique. After measuring the extent of ischaemic damage, the brain was

immediately removed from animals **treated** with or without U74006F for determination of lipid peroxidation, and the generation of free arachidonic acid in the brain. U74006F significantly ($P < 0.01$) reduced the size of ischaemic damage. Twenty-four hours after the operation, lipid peroxidation and the concentration of free arachidonic acid in the left hemisphere (infarction side) were significantly ($P < 0.05$) higher than in the right hemisphere. U74006F significantly ($P < 0.05$) decreased the content of lipid peroxidation products and free arachidonic acid. There was a significant ($P < 0.05$) correlation between the extent of ischaemic damage and the concentration of lipid peroxidation products in the left hemisphere 24 h after the operation. In conclusion, U74006F might reduce the extent of ischaemic damage by inhibiting lipid peroxidation in the brain, thus minimizing oxidative damage to neural damages.

L43 ANSWER 17 OF 18 MEDLINE
94059622 Document Number: 94059622. Microanatomy of the rat diaphragm: a **scanning** electron and confocal laser **scanning** microscopic study. Ohtani Y; Ohtani O; Nakatani T. (Second Department of Internal Medicine, Okayama University School of Medicine, Japan..) ARCHIVES OF HISTOLOGY AND CYTOLOGY, (1993 Aug) 56 (3) 317-28. Journal code: ARO. ISSN: 0914-9465. Pub. country: Japan. Language: English.
AB The present study demonstrated the three-dimensional microstructure of the rat diaphragm by **scanning** electron microscopy (SEM) of either intact or alkali-**treated tissues**, enzyme-histochemistry, and confocal laser **scanning** microscopy (LSM). The peritoneal and pleural surfaces of the diaphragm were covered with mesothelial cells studded with microvilli. Many round gaps were formed between the mesothelial cells. The submesothelial connective **tissue** contained voluminous, irregularly shaped lymphatics. Some of these lymphatics extended many funnel-like projections of their endothelia towards the pored region of the mesothelium. On coming into contact with the mesothelium, many of the lymphatic projections were perforated at their ends, thus giving rise to stomata connecting the peritoneal cavity and lymphatic lumen. Some projections ended blindly while plugging the mesothelial pores, thereby making visible some intercellular gaps in this contact. The subperitoneal sheet of the collagen fiber network possessed clusters of foramina which tightly fit the passage of the lymphatic projections. Confocal LSM of the diaphragm after intraperitoneal **injection** of FITC-dextran demonstrated the tracer both in the lymphatic lumina and in the connective **tissue** spaces. Our results indicate that peritoneal fluid is allowed to flow into the connective **tissue** spaces of the diaphragm through intercellular gaps and into lymphatics through stomata.

L43 ANSWER 18 OF 18 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
92245939 EMBASE Document No.: 1992245939. Mast cell degranulation inhibits IL-2-induced microvascular protein leakage. Edwards M.J.; Heniford B.T.; Miller F.N.. Department of Surgery, Applied Microcirculatory Res. Ctr., Louisville Univ. School of Medicine,Louisville, KY 40292, United States. Journal of Surgical Research 52/5 (429-435) 1992. ISSN: 0022-4804. CODEN: JSGRA2. Pub. Country: United States. Language: English. Summary Language: English.
AB The **therapeutic** efficacy of interleukin-2 (IL-2) in the **treatment** of cancer has been limited by a 'vascular leak syndrome' and related toxicities. To better understand the pathophysiology of the 'vascular leak syndrome,' we tested a hypothesis that mast cell degranulation mediated the acute increase in microvascular protein leakage

seen immediately following IL-2 administration. After the cremaster muscle was prepared for intravital microscopy, anesthetized Sprague-Dawley rats were **injected** with fluorescein isothiocyanate-labeled albumin for fluorescent microscopy. Animals were **treated** by the intravenous **injection** of IL-2 (1 x 106 U/kg) (n = 6), the control IL-2-vehicle (n = 5), or IL-2 (1 x 106 U/kg) after mast cell degranulation with compound 48/80 (n = 6). Relative interstitial fluorescent intensity was quantitated by a computerized **image** analysis system as an index of microvascular protein leakage. IL-2 acutely induced protein leakage from the microcirculation. Mast cell degranulation with 48/80 prior to IL-2 **treatment** prevented protein leakage, but did not alter IL-2-induced leukocyte-endothelial adherence. These data suggest that mast cell-mediated events may be responsible for the acute increase in microvascular permeability seen with IL-2 administration and that leukocyte-endothelial adherence alone is not solely responsible.

```
L44           4 FILE MEDLINE
L45           8 FILE CAPLUS
L46           6 FILE BIOSIS
L47           2 FILE EMBASE

TOTAL FOR ALL FILES
L48          20 DEES H?/AU


L49         590 FILE MEDLINE
L50         646 FILE CAPLUS
L51         845 FILE BIOSIS
L52         364 FILE EMBASE

TOTAL FOR ALL FILES
L53        2445 SCOTT T?/AU


L54           3 FILE MEDLINE
L55         113 FILE CAPLUS
L56          28 FILE BIOSIS
L57          10 FILE EMBASE

TOTAL FOR ALL FILES
L58         154 SMOLIK J?/AU


L59          75 FILE MEDLINE
L60         136 FILE CAPLUS
L61          89 FILE BIOSIS
L62          50 FILE EMBASE

TOTAL FOR ALL FILES
L63         350 WACHTER E?/AU

=> s 148 and 153 and 158 and 163

L64           0 FILE MEDLINE
L65           0 FILE CAPLUS
```

```
L66           0 FILE BIOSIS
L67           0 FILE EMBASE

TOTAL FOR ALL FILES
L68           0 L48 AND L53 AND L58 AND L63

=> dis his


     (FILE 'HOME' ENTERED AT 13:39:13 ON 09 MAR 2000)

     FILE 'REGISTRY' ENTERED AT 13:39:26 ON 09 MAR 2000
                E HALOGENATED XANTHANE/CN 5
                E ROSE BENGAL/CN 5
L1             1 S E3

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 13:49:50 ON 09
     MAR 2000
L2           381 FILE MEDLINE
L3           419 FILE CAPLUS
L4            71 FILE BIOSIS
L5           114 FILE EMBASE
L6            66 FILE WPIDS
     TOTAL FOR ALL FILES
L7          1051 S ((IODINE OR BROMINE OR HALOGENAT?)(W)XANTHENE OR L1 OR
(PHLOX
L8             0 FILE MEDLINE
L9             1 FILE CAPLUS
L10            0 FILE BIOSIS
L11            0 FILE EMBASE
L12            0 FILE WPIDS
     TOTAL FOR ALL FILES
L13            1 S L7 AND (DELIVERY VEHICLE OR MICELLE OR NANOPARTICLE OR
LIPOSO
L14            0 FILE MEDLINE
L15            0 FILE CAPLUS
L16            0 FILE BIOSIS
L17            0 FILE EMBASE
L18            0 FILE WPIDS
     TOTAL FOR ALL FILES
L19            0 S L7 AND DISEASE? TISSUE

     FILE 'REGISTRY' ENTERED AT 13:55:53 ON 09 MAR 2000
L20              STR
L21            0 S L20
L22            5 S L20 FUL
L23              STR L21
L24            0 S L23
L25              STR L23
L26           27 S L25
L27          613 S L25 FUL

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE' ENTERED AT 14:00:12 ON 09 MAR 2000
L28          548 FILE MEDLINE
L29          694 FILE CAPLUS
L30          651 FILE BIOSIS
L31          589 FILE EMBASE
     TOTAL FOR ALL FILES
L32         2482 S L27 AND (IMAG? OR XRAY OR X RAY OR CAT SCAN OR SCAN?)
L33           79 FILE MEDLINE
L34           50 FILE CAPLUS
```

```
L35           56 FILE BIOSIS
L36           87 FILE EMBASE
     TOTAL FOR ALL FILES
L37          272 S L32 AND (DELIVERY VEHICLE OR MICELLE OR NANOPARTICLE OR
LIPOS
L38            6 FILE MEDLINE
L39            3 FILE CAPLUS
L40            1 FILE BIOSIS
L41            9 FILE EMBASE
     TOTAL FOR ALL FILES
L42           19 S L37 AND (TREAT? OR THERAP?) AND (CELL MEMBRANE OR TISSUE)
L43           18 DUP REM L42 (1 DUPLICATE REMOVED)
L44            4 FILE MEDLINE
L45            8 FILE CAPLUS
L46            6 FILE BIOSIS
L47            2 FILE EMBASE
     TOTAL FOR ALL FILES
L48           20 S DEES H?/AU
L49          590 FILE MEDLINE
L50          646 FILE CAPLUS
L51          845 FILE BIOSIS
L52          364 FILE EMBASE
     TOTAL FOR ALL FILES
L53         2445 S SCOTT T?/AU
L54            3 FILE MEDLINE
L55          113 FILE CAPLUS
L56           28 FILE BIOSIS
L57           10 FILE EMBASE
     TOTAL FOR ALL FILES
L58          154 S SMOLIK J?/AU
L59           75 FILE MEDLINE
L60          136 FILE CAPLUS
L61           89 FILE BIOSIS
L62           50 FILE EMBASE
     TOTAL FOR ALL FILES
L63          350 S WACHTER E?/AU
L64            0 FILE MEDLINE
L65            0 FILE CAPLUS
L66            0 FILE BIOSIS
L67            0 FILE EMBASE
     TOTAL FOR ALL FILES
L68            0 S L48 AND L53 AND L58 AND L63

=> s (148 or 153 or 158 or 163) and (127 or 17)

L69            1 FILE MEDLINE
L70            1 FILE CAPLUS
L71            0 FILE BIOSIS
L72            0 FILE EMBASE

TOTAL FOR ALL FILES
L73            2 (L48 OR L53 OR L58 OR L63) AND (L27 OR L7)

=> dup rem 173

PROCESSING COMPLETED FOR L73
L74            2 DUP REM L73 (0 DUPLICATES REMOVED)

=> d cbib abs 1-2 hit
```

L74 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS
1987:22489 Document No. 106:22489 Development of a virtual impactor. Bartak, Josef; Hemerka, Jiri; **Smolik, Jan** (Fak. Strojni, CVUT, Prague, Czech.). Ochr. Ovzdusi, 18(9), 135-43 (Czech) 1986. CODEN: OCOVAV. ISSN: 0322-8185.
AB A math. model is given for describing a virtual impactor of the type frequently used in collecting samples of aerosols for anal. The math. relations were tested with fluorescein **[2321-07-5]** aerosols using a lab. impactor with an upper injection tube of 6.0 mm diam. and an opening of the receptor cone of 8.0 mm. The model was effective in predicting the effectiveness of particle fractionation by aerodynamic size based on the Stokes criterion.
AU Bartak, Josef; Hemerka, Jiri; **Smolik, Jan**
AB A math. model is given for describing a virtual impactor of the type frequently used in collecting samples of aerosols for anal. The math. relations were tested with fluorescein **[2321-07-5]** aerosols using a lab. impactor with an upper injection tube of 6.0 mm diam. and an opening of the receptor cone of 8.0 mm. The model was effective in predicting the effectiveness of particle fractionation by aerodynamic size based on the Stokes criterion.
IT **2321-07-5**, Fluorescein
RL: OCCU (Occurrence)
(model compds., in testing of virtual impactors for aerosol sampling and fractionation)

L74 ANSWER 2 OF 2 MEDLINE
86033941 Document Number: 86033941. Distances between the functional sites of the (Ca2+ + Mg2+)-ATPase of sarcoplasmic reticulum. **Scott T L** . JOURNAL OF BIOLOGICAL CHEMISTRY, (1985 Nov 25) 260 (27) 14421-3. Journal code: HIV. ISSN: 0021-9258. Pub. country: United States.
Language: English.
AB Luminescence energy transfer measurements have been used to determine the distances between the two high affinity Ca2+ binding-transport sites of the (Ca2+ + Mg2+)-ATPase of skeletal muscle sarcoplasmic reticulum. The lanthanide Tb3+ situated at one high affinity Ca2+ site was used as the transfer donor, and acceptors at the other Ca2+ site were the lanthanides Nd3+, Pr3+, Ho3+, or Er3+. Terbium bound to the enzyme was excited directly with a pulsed dye laser. Analysis of the changes in the terbium luminescence lifetime due to the presence of the acceptor indicates that the distance between the Ca2+ sites is 10.7 A. The distance between the Ca2+ sites and the nucleotide-binding catalytic site was determined using Tb3+ at the Ca2+ sites and either trinitrophenyl nucleotides (TNP-N) or fluorescein 5-isothiocyanate (FITC) in the catalytic site as energy acceptors. The R0 values for the Tb-acceptor pairs are approximately 30 and approximately 40 A for TNP-N and FITC, respectively. The distance between Tb3+ at the Ca2+ sites and TNP-ATP at the nucleotide site is approximately 35 A and that between the Ca2+ sites and the FITC labeling site is approximately 47 A. Considerations of the molecular dimensions of the ATPase polypeptide indicate that while the two Ca2+ sites are close to each other, the Ca2+ sites and the nucleotide site are quite remote in the three-dimensional structure of the enzyme.
AU **Scott T L**
RN **3326-32-7 (Fluorescein-5-isothiocyanate)**

=> d hitstr 1-2

NO VALID FORMATS ENTERED FOR FILE 'MEDLINE'
In a multifile environment, each file must have at least one valid format requested. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> select hit

ENTER ANSWER SET OR SMARTSELECT L# OR (L74):170

ENTER ANSWER NUMBER OR RANGE (1-):.

ENTER DISPLAY CODE (TI) OR ?:rn

E1 THROUGH E1 ASSIGNED

=> fil reg;s e1;d ide can

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	142.33	481.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.67	-4.88

FILE 'REGISTRY' ENTERED AT 14:08:25 ON 09 MAR 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 8 MAR 2000 HIGHEST RN 258533-18-5
DICTIONARY FILE UPDATES: 8 MAR 2000 HIGHEST RN 258533-18-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

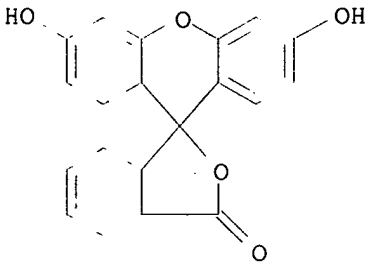
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

L75 1 2321-07-5/BI
(2321-07-5/RN)

L75 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN **2321-07-5** REGISTRY
CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 3',6'-dihydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Fluorescein (8CI)
OTHER NAMES:
CN 3',6'-Dihydroxyfluoran
CN 3',6'-Fluorandiol
CN 3,6-Dihydroxyspiro[xanthene-9,3'-phthalide]

CN Benzoic acid, 2-(6-hydroxy-3-oxo-3H-xanthen-9-yl)-
CN C.I. 45350:1
CN C.I. Solvent Yellow 94
CN D and C Yellow No. 7
CN Fluorescein acid
CN Japan Yellow 201
CN Japan Yellow No. 201
CN Resorcinolphthalein
CN Solvent Yellow 94
CN Yellow fluorescein
AR 518-45-6
FS 3D CONCORD
DR 126605-73-0, 213880-86-5
MF C20 H12 O5
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



3283 REFERENCES IN FILE CA (1967 TO DATE)
688 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3300 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 132:144389

REFERENCE 2: 132:134307

REFERENCE 3: 132:132319

REFERENCE 4: 132:131472

REFERENCE 5: 132:129811

REFERENCE 6: 132:127457

REFERENCE 7: 132:122104

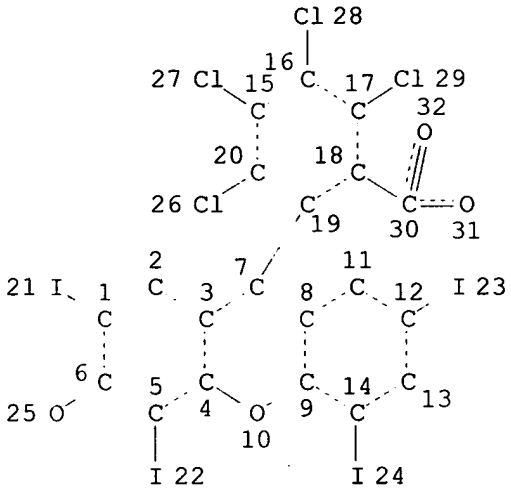
REFERENCE 8: 132:118027

REFERENCE 9: 132:110235

REFERENCE 10: 132:108597

=> d l78 que stat

L76 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L78 0 SEA FILE=REGISTRY SSS FUL L76

100.0% PROCESSED 105 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

=> del hi sy

HI IS NOT VALID HERE
The DELETE command is used to remove various items stored by the system.

To delete a saved query, saved answer set, saved L-number list, SDI request, batch request, mailing list, or user-defined cluster, format, or search field, enter the name. The name may include ? for left, right, or simultaneous left and right truncation.

Examples:

```
  DELETE BIO?/Q          - delete query names starting with BIO
  DELETE ?DRUG/A         - delete answer set names ending with DRUG
  DELETE ?ELEC?/L        - delete L-number lists containing ELEC
  DELETE ANTICOAG/S      - delete SDI request
  DELETE ENZYME/B        - delete batch request
  DELETE .MYCLUSTER      - delete user-defined cluster
  DELETE .MYFORMAT       - delete user-defined display format
```